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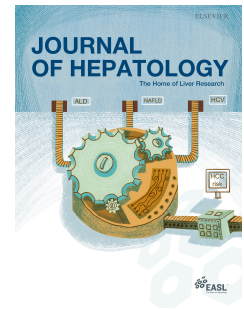
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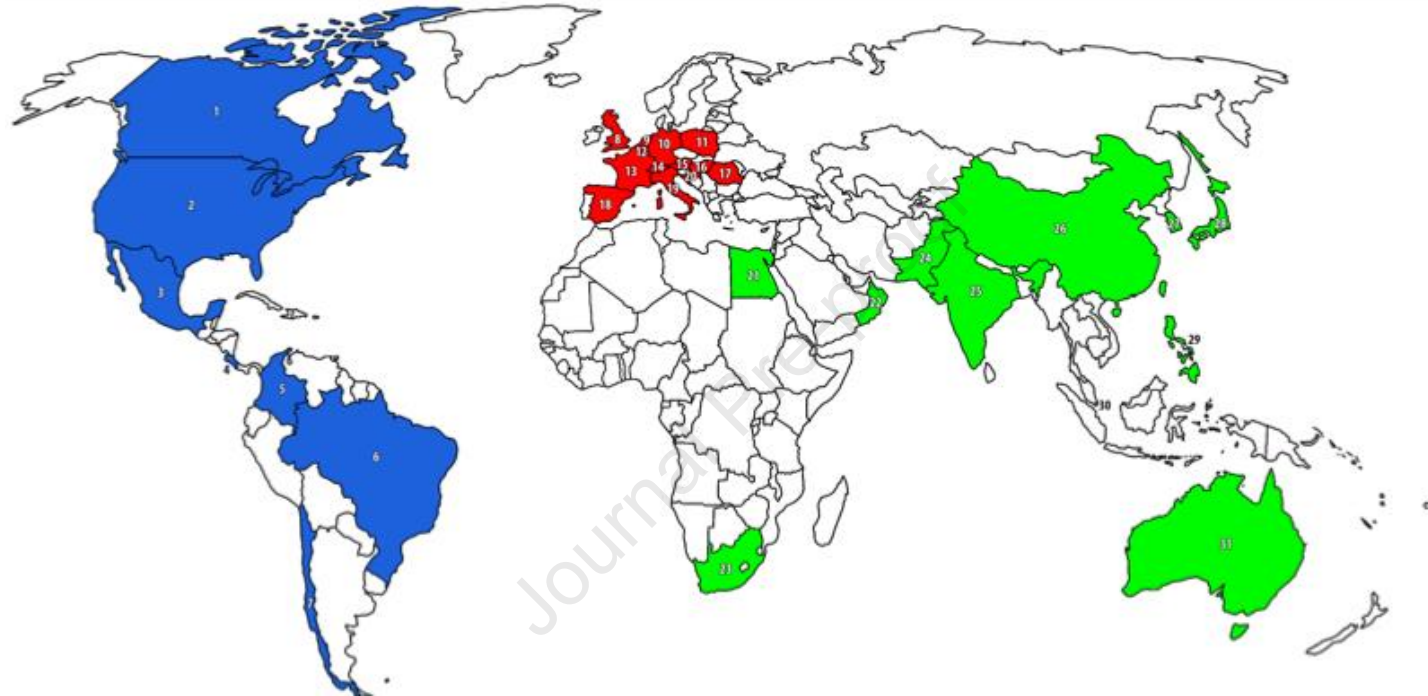
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# The global impact of the first wave of COVID-19 on liver transplant centers: A multi-society survey



## **Global impact of the first wave of COVID-19 on liver transplant centers: A multi-society survey (EASL-ESOT/ELITA-ILTS)**

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**Authors' contributions**

All authors made substantial contributions to the conception and design, the acquisition, analysis, and interpretation of the data, FPR, MI, AS, VAK, TDM drafted the article and made critical revisions for important intellectual content. TDM performed statistical analysis. All authors approved the version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the article are appropriately investigated and resolved.

**Data Availability statement:**

The data that support the findings of this manuscript are available from the corresponding author

## Abstract

**Background and Aims:** The global impact of SARS-CoV-2 on liver transplantation (LT) practices across the world is unknown. The goal of this survey was to assess the impact of the pandemic on global LT practices.

**Method:** A prospective web-based survey (available online from 7<sup>th</sup> September 2020 to 31<sup>st</sup> December 2020) was proposed to the active members of the EASL-ESOT/ELITA-ILTS in the Americas (including North, Central, and South America) (R1), Europe (R2), and the rest of the world (R3). The survey comprised four parts concerning the transplant processes, therapy, living donor, and organ procurement.

**Results:** Of the 470 transplant centers reached, 128 answered each part of the survey, 29 centers (23%), 64 centers (50%), and 35 centers (27%) from R1, R2, and R3, respectively. When we compared the practices during the first six months of the pandemic in 2020 with that a year earlier in 2019, statistically significant differences were found in the number of patients added to the waiting list (WL), the number of WL mortality, and the number of transplantations. At the regional level, we found that in R2 the number of LTs was significantly higher in 2019 ( $p < 0.01$ ), while R3 had more patients listed, higher WL mortality, and more LTs performed before the pandemic. Countries severely affected by the pandemic (“hit” countries) had a lower number of WL patients ( $p = 0.009$ ) and LT ( $p = 0.002$ ) during the pandemic. Interestingly, WL mortality was higher in the pandemic in “non-hit” countries ( $p = 0.022$ ) compared to 2019.

**Conclusion:** The first wave of the pandemic differentially impacted LT across the world, especially with detrimental effects on the “hit” countries. The modifications in the policies for recipient and donor selection, organ retrieval, and postoperative recipient management were adopted at a regional or national level.

**Lay summary**

The health emergency caused by the Coronavirus has dramatically changed clinical practice during the pandemic.

The first wave of pandemic impacted Liver Transplantation across the world differently, especially with detrimental effects on the hit countries

The resilience of the entire transplant network has enabled the support of organ donations and transplants to ultimately improve the lives of patients with end-stage liver disease

## Introduction

In late 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in China as a serious threat to public health (1). Since then, SARS-CoV-2 has become a devastating pandemic that has remarkably overwhelmed the healthcare systems around the world, resulting in more than 168 million infections with a death toll exceeding 3.5 million as of May 2021 (2). Additionally, the collateral damage of the SARS-CoV-2 pandemic has been extensive, disrupting the management of acute and chronic diseases globally (3–5).

The early days of the pandemic had demonstrated that SARS-CoV-2 affected liver transplantation at the level of the infrastructure, as well as the individual patient and provider (6). The operation of the liver transplantation (LT) program, including evaluation and selection of potential candidates, wait-list management, donor evaluation, transplantation, and subsequent recipient and living donor follow-up, requires substantial resources and infrastructure that were compromised, especially early in the pandemic as demonstrated by few regional studies (7). In countries with primarily deceased donations, the situation was further complicated as individual liver transplant programs depend on the donor networks to continue liver transplantation (8). Patients with cirrhosis (9) and recipients of liver transplants (10) are thought to be at a higher risk of morbidity and mortality from SARS-CoV-2. Liver donor to recipient transmission has also been reported (11). Frontline healthcare workers have been at a higher risk of SARS-CoV-2 infection (12), causing a large proportion of the workforce to be temporarily out of

service. These factors have led liver transplant centers worldwide to adopt various strategies hoping to mitigate the risk of their patients and liver transplant care providers. These strategies involved every aspect of the liver transplant process, including managing infected or exposed patients on the wait-list, pausing or limiting transplant and donor operations, implementing new policies regarding retrieval of the donated organs, adjusting post-transplant immunosuppression, and adopting virtual technology for patient follow-up, among other policies (13). Currently, there is insufficient data on the changes in these practices and/or risk mitigation approaches and policies. Therefore, a task force was formed in mid-2020 by the European Association for the Study of Liver disease (EASL), International Liver Transplantation Society (ILTS), and the European Liver and Intestine Transplant Association (ELITA) of the European Society of Organ Transplantation (ESOT) to investigate the global impact of the first wave of the SARS-CoV-2 pandemic on liver transplant centers and their patient care practices by a multidisciplinary online survey. Here, we report the results of the survey and their implications, which may help the liver transplant centers to operate better if they continue to encounter the sequelae of the current pandemic and optimize these programs for future pandemics.

## Methods

A prospective cross-sectional web-based survey (available online from 7<sup>th</sup> September 2020 to 31<sup>st</sup> December 2020) was designed by a group of investigators dedicated to the care of patients in need of liver transplants from three international societies: EASL, ESOT-ELITA, and ILTS. The survey was created using Google Forms (Google LLC, Mountain View, CA, USA) and consisted of single-choice items and open-answer questions.

The study protocol conformed to the ethical guidelines and was approved by the institutional review board of Vanderbilt University Medical Center, USA. The survey was available on the websites of all three societies, and all members of the societies were invited by email to respond, ensuring not to duplicate the emails or the personnel at each center. The survey was also promoted via social media platforms (Twitter and Facebook accounts of the participating societies). The

participants were given a choice to disclose their transplant center names and contact information, and 97% of the participants disclosed the information. Non-respondents were contacted at least twice.

The survey was divided into four independent parts. Section 1 assessed the influence of the pandemic on LT programs across the globe, evaluating different topics such as wait-listing, transplant volumes, mortality, and others, compared to that in the same period in the previous year. Section 2 evaluated the impact of special precautions, modifications, and demands required for the continuation of services during the first wave of the pandemic. Section 3 dealt with different aspects of living donations during the pandemic. Finally, Section 4 highlighted the effects of the pandemic on deceased liver donations, especially regarding strategies to recover organs (Supplementary Section 1).

Data was collected and categorized into three regions: the Americas (including North, Central, and South America) (R1), Europe (R2), and the rest of the world (R3).

### **Statistical Analysis**

Data was expressed as a median and interquartile range, while categorical variables were expressed as percentages. Continuous variables were compared by unpaired Student's T-test, Mann-Whitney U-test, or Wilcoxon signed paired test for related variables. Distribution was assessed by normality plots and the Shapiro-Wilk test. Categorical variables were compared by determining  $X^2$  values by performing Fisher's exact test. Trends in the number of patients listed for liver transplantation, mortality in the waiting list, and the number of liver transplants performed between similar periods before and after the pandemic were expressed as a ratio (e.g., variable between 1st January and 1st July in 2019/variable between 1st January and 1st July in 2020) and changes were assessed by multivariable linear regression after adjusting for COVID19 case-fatality rate, living donor activity and country. Analysis of subgroups was performed for assessing outcomes according to the continents "hit" versus "non-hit" countries, and volume of living donor activity. Continents were classified as Africa (Egypt, South Africa); the Americas (Brazil, Canada, Chile, Colombia, Costa Rica, Mexico, the United States of America); Asia (China, India, Japan, Jordan, Oman,

Pakistan, the Republic of the Philippines, Singapore, South Korea); and Europe (Austria, Belgium, Croatia, France, Germany, Hungary, Italy, Netherlands, Poland, Portugal, Romania, Russia, Spain, Switzerland, Turkey, the United Kingdom). In order to define “hit” and “non-hit” countries a Multivariate Adaptive Regression Splines (MARS) was modeled considering 3 gradients per spline in order to define the best cut-off explaining a change in the trend of the number of patients listed for LT, mortality in the waiting list, and the number of LT performed pre- and post- pandemic periods according with the case-fatality rate of COVID19 across the countries, see Supplementary Section 2 Figure 1 (data obtained from the World Health Organization, <https://covid19.who.int>). The best cut-off was chosen, and Bayesian credibility intervals were assessed. Centers with more than 30% of LDLT per year were considered as having a high volume of LDLT activity. Post hoc Bayesian credibility intervals and correction for multiple comparisons were performed by the Bonferroni test. Missing data was treated by list-wise deletion. All statistical analyses were performed with STATA 15/IC.1 (StataCorp. 2017; Stata Statistical Software: Release 15; College Station, TX: StataCorp LLC).

## Results

### Transplant processes

A total of 470 liver transplant centers were reached across the world. Among these, 128 centers responded by filling all parts of the survey. This included 29 centers (23%), 64 centers (50%), and 35 centers (27%) from R1, R2, and R3, respectively (Figure 1 and Supplementary section 3 Table1).

Most hospitals (62.1–71.4%) across the globe had specific areas dedicated to COVID, and very few remained COVID-free hospitals. Most transplant centers withheld Donor Deceased Liver Transplantation (DDLTL) services for up to a month (R1 = 45.5%, R2 = 50%, and R3 = 28.6%). Nevertheless, acute liver failure (ALF) remained an exemption to this hold (R1 = 52.6%, R2 = 54.8%, and R3 = 31.2%), and patients were managed in most centers on a case-by-case basis.

Globally, 30–50% of the centers performed transplants on recipients with a previous diagnosis of COVID-19 (R1: 52.4%, R2: 28.8, and R3: 29.4%).

About 30% of the centers reported that fear of COVID was the cause of the denial of the transplant proposal.

Comparing the overall transplant practices across the globe during the first six months of the pandemic with the corresponding period from 2019 revealed significant differences in the lower number of wait-listed candidates (32.5% vs 60.7%,  $p=0.004$  in 2020 vs 2019, respectively), higher wait-list mortality (52.3% vs 26.1%,  $p=0.006$ ) and the lower number of LT (36.4 % vs 59.5%,  $p=0.001$ ) (Table 1). A further sub-analysis to assess the impact of the geographical heterogeneity of the pandemic on regional LT services across countries and continents showed that Asia had fewer wait-listed patients in 2020 than at a similar period in the previous year (33.3% vs 63.3%,  $p = 0.040$ ) (Table 2). Europe also showed a non-significant trend with fewer wait-listed patients in 2020 (59.4% and 31.3% centers in 2019 and 2020, respectively) (Table 2). In 2020, the wait-list mortality was higher in Asia (58.6% vs 20.7%,  $p = 0.041$ ), while Europe showed a non-significant trend (27.4% vs. 51.6% centers with a mortality rate in 2019 and 2020, respectively) (Table 2). Correspondingly, a higher number of LT were performed in 2019 than in 2020 in Asia and Europe ( $p = 0.011$  for both continents), while these trends were not observed in the Americas (Table 2). However, corrections for post hoc comparisons showed no significant difference across the continents (corrected significance of  $p\text{-value} \leq 0.006$ ). With low respondents from Africa and Australia, these continents were excluded from the analyses (Table 2, Supplementary Section 2 figure 2).

Out of the 33 countries, Egypt had a greater number of patients listed in 2019 than in 2020 ( $\beta$  3.386, CI95% 0.963; 5.808,  $p=0.007$ ). India and Mexico had a similar trend ( $\beta$  2.011, CI95% -0.871; 4.109,  $p=0.060$  and  $\beta$  2.163, CI95% -0.259; 4.585,  $p=0.079$ , respectively). The ratio of LT performed in 2019 compared to that in 2020 was significantly higher in India, Oman, and the Philippines ( $\beta$  2.470, CI95% 0.1208; 4.820,  $p=0.040$ ;  $\beta$  8.121, CI95% 4.940; 11.303  $p < 0.001$  and 3.288, CI95% 0.106; 6.469,  $p= 0.043$ , respectively) than in the other countries. These results were confirmed by



Bayesian inference (Supplementary Section 3 Table 2).

### **“Hit” vs. “non-hit” countries**

COVID19 case-fatality rate of 3.4% was considered the best cut-off for “hit” versus “non-hit” countries with a 95% of probability to fall between 0.028 and 0.051 bounds based on the main outcomes of liver transplant activity.

“Hit” countries had a lower number of waitlisted patients (29.2% vs 66.7%,  $p=0.009$  in 2020 vs 2019, respectively) and LT (25% vs 47.9%,  $p=0.002$ ) (table 3) during the pandemic when compared to a similar period in 2019. Moreover, the “non-hit” countries had a similar number of waitlisted patients (34.8% vs 56.5%,  $p=0.097$ ) and LT numbers (43.8% vs 52.1%,  $p=0.109$ ) (table 3) during the pandemic as compared to 2019. Interestingly, the pre-pandemic mortality rate in wait list was higher in the “non-hit” countries than in the “hit” countries (54% vs 24.4%,  $p=0.022$  and 50% vs 27.1%,  $p=0.124$ , respectively). However, only waitlisted patients and the number of LT performed in “hit countries” were significantly diminished in pandemic era after post hoc comparison correction (corrected  $p\text{-value} \leq 0.013$ ) (Supplementary Section 2 Figure 3).

### **Living Donor Liver Transplantation (LDLT)**

Another subgroup analysis of LDLT centers categorized as low volume ( $\leq 30\%$  LDLT activity) and high volume ( $> 30\%$  LDLT activity) showed that the influence of the pandemic was more obvious in high volume LDLT centers. There were significantly fewer wait-listed patients (27% vs 70.3%,  $p=0.005$  in 2020 vs 2019) (Table 4) and fewer LTs performed in high volume LDLT centers (35% vs 62.5%,  $p=0.013$ ) (Table 4) after the pandemic compared to that in 2019. The “low volume” LDLT centers were predominantly from the Americas and Europe and had a similar number of wait-listed patients, but a lower number of LTs performed in 2020 compared to that in 2019 (34.7% vs 59.7%,  $p=0.006$  in 2020 vs 2019, respectively). However, the wait-list mortality in both high and low volume LDLT centers was similar across the two periods (57.1% vs 25.7%,  $p=0.089$  and 47.8% vs 29%,  $p=0.123$ , respectively) (Table 4). Moreover, the waitlist mortality was not associated with COVID19 case-fatality rate once adjusted for country and LDLT activity. Data was confirmed after

post hoc comparison correction (corrected significance of  $p\text{-value} \leq 0.013$ ) (Supplementary Section 2 Figure 4)

### **Organ Donation**

Most transplant teams ( $R1 = 83.3\%$ ,  $R2 = 42.6\%$ , and  $R3 = 44.1\%$ ) made specific policy changes to their organ recovery protocols for safety during the pandemic. Only 12–17% of the centers transplanted organs from previously SARS-CoV-2 infected donors, mostly when the disease-to-donation interval was over a month. Four LDLT donors from R1 and R3 were diagnosed with COVID19 in the postoperative period. Three of them had an uneventful course and were discharged; no data were available on the 4<sup>th</sup> donor.

### **Recipient Outcomes**

Between 18.2% and 36.4% of the recipients tested positive for SARS-CoV-2 after LT with a mortality rate of  $R1 = 25\%$ ,  $R2 = 20\%$ , and  $R3 = 8.3\%$  across the three regions. Only 23% of the centers retested donors/recipients for COVID at discharge.

### **Immunosuppression and anticoagulation**

Only 8–14% of the centers routinely reduced Calcineurin Inhibitors (CNI) in LT recipients following COVID infection. Most centers managed immunosuppression on a case-by-case basis (52.8–75%). The regular use of anticoagulants in recipients differed significantly across the three regions ( $R1 = 45.8\%$ ,  $R2 = 38.2\%$ , and  $R3 = 64.3\%$ ;  $p = 0.03$ ).

### **Telemedicine**

Nearly all transplant centers depended heavily on virtual technology during the pandemic, and very few centers did not use telemedicine ( $R1 = 0\%$ ,  $R2 = 12.3\%$ , and  $R3 = 14.3\%$ ).

### **Discussion**

SARS-CoV-2, an invisible microorganism, has put the whole world under pressure, with devastating health, human and economic costs (14). Yet, it is crucial to recognize that the frequency of pandemics have increased over the past twenty years and it is unlikely that SARS-CoV-2 will be

the last global health crisis that we witness, as discussed by Drs. Morens and Fauci in their recent publication “Emerging Pandemic Diseases: How We Got to COVID-19”. (15). Therefore, the lessons learned from the current pandemic including the impact on the individual areas of medical practice could be critical knowledge for the future in the instance of the new health crisis.

Although it has been recognized that SARS-CoV-2 pandemic had a profound impact on the healthcare system, data about the global impact of the virus on LT practices across the world are limited.

The survey showed an early cessation of activity in LT centers, generally for four weeks. However, an exception was made for the patients referred to the centers in severe conditions (acute liver failure, high MELD, and acute or chronic liver failure). Before the first wave, little was known regarding the impact of an immunosuppressed state on COVID-19 and vice-versa, and most recommendations were extrapolated from previous SARS/MERS epidemics. Scientific evidence remained scarce and strategies were based only on expert opinion. This is also reflected in results of our survey, wherein there remained a heterogeneity in the answers with regards to transplantation of infected patients, their ‘cooling off’ period, and the urgency of operation. In those more uncertain times, based on available evidence, various transplant societies across the world came up with their recommendations (16-20). Interestingly, a study based on consensus-based guidance derived from individual information of 22 transplant societies highlighted a high degree of consensus (21). 14 of 19 societies recommended either a temporary suspension or reduction of elective transplantation to a minimum. It was recommended that the decision to LT should be done on a case-to-case basis, giving priority to those who were unstable or had a MELD of over 25 or 30. Furthermore, a relaxation of rules was based on the availability of ICU beds and staff required for the transplantation procedure. More recently, strong evidence-based data such as from the ELITA/ELTR cohort corroborate previously suggested recommendations with regards to the urgency and safety of transplanting high MELD patients (22). Furthermore, reducing transplantation activities allowed the establishment of necessary COVID-19 wards, freeing the

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management of COVID-19-affected critically ill patients, and allowing the mobilization of health personnel (both medical and non-medical) to COVID-19 affected areas.

Interestingly in some cases, patients on the waiting list for a transplantation denied their consensus to the transplantation for fear of being infected, probably due to more somatization symptoms. We can consider transplant patients with a higher vulnerability and an impaired self-awareness, needing more information about their illness, about the possible changes and fears associated with the spread of an infectious disease, their medication and treatment strategies for stress reduction in addition to receiving more information about how to protect themselves from being infected with SARS-CoV2 (23). Based on the fears and information deficits reported by patients in a German survey (24), transplant centers are advised to intensify communication strategies and consider implementing telehealth in order to provide optimum medical care in liver transplant recipients and patients on the waiting list. As underlined by Holmes et al (25), feeling distressed or anxious is understandable for many going through such unprecedented times. Clearly, for those who are vulnerable, it is important to be vigilant to mitigate the risks to mental health difficulties. We also need to consider longer term preventive approaches more broadly, so that we are more responsive to the chronic outcomes of the current pandemic as well as being better prepared for future public health crises.

As expected, the regions most affected by the pandemic were the ones that had fewer patients added to the wait-list for transplantation and fewer transplants performed in the first six months of 2020 compared to that in 2019. However, the survey showed an interesting result, a higher WL mortality in non-hit countries compared to hit countries. This could have been due to the severe lockdown in these regions during the pandemic. This hypothesis fits with another interesting result in our survey, i.e., the areas with high living transplant activity had more patients added in the WL and more LTs performed in 2019 compared to that in 2020. Although, cessation of transplant activity during pandemic especially in the setting of living donation is prudent, the special attention should be paid to sick patients on the WL. If increased WL mortality in non-hit countries during

pandemic were the result of the severe lock-down or the fear of seeking the medical care due to the potential exposure, the findings would support the concerns of unrecognized collateral damage from the pandemic to our society and warrants a reassessment of how we manage the patients with chronic liver disease at the time of pandemic. (25-27)

In the survey, only a percentage of the transplant centers decided to consider previous positive candidates for transplantation. In a recent international series (22), patients with prior COVID-19 had favorable outcomes, with early survival of 96% (25/26) after receiving a liver transplant. Median ICU and total hospital stay were 3 (IQR 3–6) and 11 (IQR 8–19) days, which concur with what is observed in more recent series (28). The ideal timing for readmission of patients to the transplant waiting list is not yet clear, however in clinical practice at the moment most of the guidelines suggest to consider the patients after at least 2 weeks since the negative swab.(29-30). However, a negative RT-PCR rhinopharyngeal swab and an additional negative swab at the time of LT should be enough to readmit the patient in the waiting list, because to date, zero cases of SARS-CoV-2 recurrence was observed after LT. With the paucity of data, it is not known if patients recently affected by COVID-19 can be safely transplanted.

Immunosuppression in these patients may result in adverse outcomes, and the optimal disease-free interval is currently unknown (31-35). For the reduction of immunosuppression to prevent SARS-CoV-2 infection, most centers evaluated recipients on a case-by-case basis. The EASL guidelines confirmed these findings, suggesting that reduction should only be considered under special circumstances (*e.g.*, medication- induced lymphopenia or bacterial/fungal superinfection in case of severe COVID-19) (36). The results from the ELITA-ELTR multicenter study demonstrated that the use of tacrolimus was associated with better survival in 243 symptomatic liver transplant recipients (37). Recent data from Spanish transplant centers showed that the baseline immunosuppression using mycophenolate was an independent predictor of severe COVID-19 and it was dose-dependent(38).

We also found a discrepancy in the prophylactic use of subcutaneous anticoagulants to prevent thromboembolism. In most of the European centers and few centers from other regions, heparin or heparin-like drugs were routinely administered in transplant patients.

Another issue raised by the survey was whether donors/recipients were tested for Sars-CoV-2 at discharge. Most of the transplant centers, did not check the infection, because, as suggested by the survey, transplant patients were hospitalized in COVID-free areas, where both patients and health personnel were subjected to serial swabs. Most of the transplant centers adopted the policy to repeat the swab at the time of discharge only if the patient was symptomatic or for specific reasons.

Our survey has some limitations. Given a rapid development of the pandemic that placed an extraordinary burden on the healthcare providers, the overall response rate for our survey was only 27%, ranging between 23-50%; however, the authors felt that the timely report on specific practices by transplant centers in different world regions during the first wave of pandemic was a valuable addition to the transplant literature. Particularly, as the world lives through the recurrent waves of pandemic, the information from our report may alert the transplant centers to the processes of WL activation, management, and transplant decisions. First of all, the impact of the first wave of Sars-CoV-2 infection was different across the world, so it is difficult to compare the consequences at a global level. Another limitation of the survey is that unfortunately we do not have the absolute number of patients belonging to the centers that responded, but the percentages of responses of colleagues who report their experience. Even with a large number of responses, we cannot exclude a global underestimation of the impact of COVID-19 in the transplant setting. Finally, while analyzing the data at a global scale, we cannot exclude missing some peculiarities of the impact of the infection at a local scale. Specifically, center-based COVID-related epidemiologic data was not available at the time of the study. Therefore, the analyses were done based on the available country- or state-based data.”

Nevertheless, our study has strengths, including real-time data collection by the international multi-society collaborative survey regarding the impact of the first wave of Sars-CoV-2 infection on

liver transplant activity across the globe. Importantly, the global nature of this study offered a unique opportunity to demonstrate intercontinental and interregional differences in liver transplant-related outcomes and practices. Furthermore, these observations may serve as lessons for liver transplant programs to learn from upon handling future waves of this pandemic, other pandemics, or other hurdles of this magnitude.

In conclusion, this international survey suggests that the first wave of pandemic impacted LT across the world differently, especially with detrimental effects on the hit countries. However, the survey has shown the resilience of the entire transplantation network to support liver donation and transplantation to improve the lives of patients with end-stage liver disease ultimately.



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## TABLES

	<b>Global</b>		
	2019	2020	p value
Centers with higher listed patients	60.7%	32.5%	<b>0.004</b>
Center with higher mortality in WL	26.1%	52.3%	<b>0.006</b>
Center with higher LT performed	59.5%	36.4%	<b>0.001</b>

Table 1 Center with higher number of listed patients, higher mortality in the WL for LT and higher LT performed, comparing 2019 vs 2020, the global results are shown.

	<b>R1</b>			<b>R2</b>			<b>R3</b>		
	2019	2020	p value	2019	2020	p value	2019	2020	p value
Centers with higher listed patients	60.0%	35.0%	0.490	59.4%	31.3%	0.072	63.3%	33.3%	<b>0.040</b>
Center with higher mortality in WL	23.5%	47.1%	0.301	27.4%	51.6%	0.100	20.7%	58.6%	<b>0.041</b>
Center with higher LT performed	52.4%	42.9%	0.958	59.4%	35.9%	<b>0.011</b>	63.6%	33.3%	<b>0.011</b>
				<b>Corrected p-value was <math>\leq 0.006</math></b>					

Table 2 Center with higher number of listed patients, higher mortality in the WL for LT and higher LT performed, comparing 2019 vs 2020, the results divided for geographic area (R1: Americas, R2.

Europe, R3: rest of the world).

	<b>Non-Hit countries</b>			<b>Hit countries</b>		
	2019	2020	p value	2019	2020	p value
Centers with higher listed patients	56.5%	34.8%	0.097	66.7%	29.2%	<b>0.009</b>
Center with higher mortality in WL	25.4%	54.0%	<b>0.022</b>	27.1%	50.0%	0.124
Center with higher LT performed	52.1%	43.8%	0.109	47.9%	25.0%	<b>0.002</b>
				<b>Corrected p-value was <math>\leq 0.013</math></b>		

Table 3 Center with higher number of listed patients, higher mortality in the WL for LT and higher LT performed, comparing 2019 vs 2020 in hit vs non-hit countries

	Low LDLT activity			High LDLT activity		
	2019	2020	p value	2019	2020	p value
Centers with higher listed patients	57.7%	33.8%	0.100	70.3%	27.0%	<b>0.005</b>
Center with higher mortality in WL	29.0%	47.8%	0.123	25.7%	57.1%	0.089
Center with higher LT performed	59.7%	34.7%	<b>0.006</b>	62.5%	35.0%	<b>0.013</b>
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Table 4 Center with higher number of listed patients, higher mortality in the WL for LT and higher LT performed, comparing 2019 vs 2020 in low LDLT activity vs high LDLT activity



**R2**  
 8: Sweden, Gothenburg  
 9: United Kingdom: Birmingham, Cambridge, Edinburg, Leeds, Manchester, Newcastle  
 10: The Netherlands: Groningen, Rotterdam  
 11: Germany: Berlin, Essen, Frankfurt, Hamburg, Hannover, Homburg-Saarland, Jena, Kiel, Leipzig, Muenster, Tübingen  
 12: Poland: Katowice, Warsaw  
 13: Belgium: Brussels, Gent, Liege

**14: France: Montpellier, Strasbourg**  
**16: Austria: Vienna**  
**17: Hungary: Budapest**  
**18: Romania: Bucharest**  
**19: Portugal, Coimbra**

**20: Spain: Alicante, Barcelona Hospital Clinic, Barcelona Vall d'Hebron, Bilbao, Cordoba, La Coruña, Madrid, Murcia, Pamplona, Santander, Seville, Valencia, Valladolid, Zaragoza**  
**21: Italy: Bari, Bergamo, Bologna, Cagliari, Genova, Milan Niguarda, Milan Policlinico, Milan NTI, Modena, Naples, Padua, Palermo, Pisa, Roma Gemelli, Roma La Sapienza, Roma Tor Vergata, Torino, Udine**  
**22: Croatia, Zagreb**

**R 1**  
**1: Canada**  
 - Edmonton  
 - Montréal  
 - Toronto  
**2: United States of America**  
 - California: Paolo Alto, San Diego  
 - Connecticut: New Haven  
 - Iowa: Iowa City  
 - Illinois: Chicago  
 - Minnesota: Minneapolis  
 - New York: New York  
 - Tennessee: Nashville  
 - Texas: Houston  
**3: Mexico, Mexico City**  
**4: Costa Rica San Jose**  
**5: Colombia, Cali**  
**6: Brazil**  
 - Campinas  
 - Ribeirão Preto  
 - Sao Paulo,  
**7: Chile, Santiago**

**R 3**  
**23: Russia: Moscow**  
**24: Turkey: Ankara and Bursa**  
**25: Pakistan: Gambat, Islamabad**  
**26: China and Hong Kong: Hangzhou, Shanghai and Hong Kong**  
**27: South Korea, Daejeon**  
**28: Japan: Chiba, Fukuoka, Hiroshima, Kobe, Kyoto, Matsumoto, Nishihara, Okinawa, Sapporo, Tokyo, Toon**  
**29: Egypt, Cairo, Shebin Alkawn**  
**30: Jordan, Amman**  
**31: Oman, Muscat**  
**32: India: Ahmedabad, Chennai, Delhi, Gurugram, New Delhi, Hyderabad, Mumbai**  
**33: Philippines: Metro Manila**  
**34: Singapore**  
**35: South Africa, Johannesburg**  
**36: Australia, Melbourne**

**Figure 1: the list of centers that contributed to the survey**

## TABLES

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<b>The difference of percentage for reaching 100% is representing the centers with same activity in 2019 and 2020: E.g: 60.7% of centers had a higher number of listed patients in 2019; 32.5% had a higher number of listed patients in 2020 and 6.8% had the same number of listed patients.</b>			

Table 1 Center with higher number of listed patients, higher mortality in the WL for LT and higher LT performed, comparing 2019 vs 2020, the global results are shown.

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Table 4 Center with higher number of listed patients, higher mortality in the WL for LT and higher LT performed, comparing 2019 vs 2020 in low LDLT activity vs high LDLT activity

- Liver transplantation was severely affected in every aspect by SARS-CoV2 pandemic
- An international multi-society taskforce evaluated the real impact of SARS-CoV2's first wave
- The pandemic detrimentally impacted transplant operations in heavily hit countries
- Transplant centers' resilience led to efficient accommodations in clinical practice
- These observations may serve to handle future emergencies of this magnitude